

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
28 October 2004 (28.10.2004)

PCT

(10) International Publication Number  
**WO 2004/092383 A3**

(51) International Patent Classification<sup>7</sup>: C12N 15/11, A61K 31/713

(21) International Application Number:  
PCT/US2004/011320

(22) International Filing Date: 13 April 2004 (13.04.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/462,874 15 April 2003 (15.04.2003) US  
10/427,160 30 April 2003 (30.04.2003) US  
10/444,853 23 May 2003 (23.05.2003) US  
10/693,059 23 October 2003 (23.10.2003) US  
10/720,448 24 November 2003 (24.11.2003) US  
10/757,803 14 January 2004 (14.01.2004) US

(71) Applicant (for all designated States except US): SIRNA THERAPEUTICS, INC. [US/US]; 2950 Wilderness Place, Boulder, CO 80301 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): MCSWIGGEN, James [US/US]; 4866 Franklin Dr., Boulder, CO 80301 (US). BHARAT, Chowira [US/US]; 576 Manorwood Lane, Louisville, CO 80027 (US). HAEBERLI, Peter [US/US]; 705 7th Street, Berthoud, CO 80513 (US).

(74) Agent: GREENFIELD, Michael, S.; McDonnell Boehnen Hulbert and Berghoff, Suite 3100, 300 S. Wacker Drive, Chicago, IL 60606 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:  
10 February 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: RNA INTERFERENCE MEDIATED INHIBITION OF SEVERE ACUTE RESPIRATORY SYNDROME (SARS) VIRUS GENE EXPRESSION USING SHORT INTERFERING NUCLEIC ACID (siNA)

(57) Abstract: The present invention comprises compounds, compositions, and methods useful for modulating the expression of genes associated with respiratory and pulmonary disease, such as severe acute respiratory syndrome (SARS) virus genes, using short interfering nucleic acid (siNA) molecules. This invention also comprises compounds, compositions, and methods useful for modulating the expression and activity of SARS virus genes, or other genes involved in pathways of SARS virus gene expression and/or activity by RNA interference (RNAi) using small nucleic acid molecules. In particular, the instant invention features small nucleic acid molecules, such as short interfering nucleic acid (siNA), short interfering RNA (siRNA), double-stranded RNA (dsRNA), micro-RNA (miRNA), and short hairpin RNA (shRNA) molecules and methods used to modulate the expression of SARS virus RNA.

WO 2004/092383 A3

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2004/011320

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C12N15/11 A61K31/713

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>PEIRIS J S M ET AL: "Coronavirus as a possible cause of severe acute respiratory syndrome."  LANCET (NORTH AMERICAN EDITION),  vol. 361, no. 9366,  8 April 2003 (2003-04-08), pages  1319-1325, XP002310168  ISSN: 0099-5355  Published online on 8. 4. 2003  (<a href="http://image.thelancet.com/extras/03art3477web.pdf">http://image.thelancet.com/extras/03art3477web.pdf</a>)  page 1322, left-hand column, paragraph 2 -  page 1323, left-hand column, paragraph 3</p> <p style="text-align: center;">----- -/--</p>	1-31

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*G\* document member of the same patent family

Date of the actual completion of the international search

23 December 2004

Date of mailing of the international search report

05/01/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Barnas, C

# INTERNATIONAL SEARCH REPORT

In **na**l Application No  
PCT/US2004/011320

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>KSIAZEK THOMAS G ET AL: "A novel coronavirus associated with severe acute respiratory syndrome." NEW ENGLAND JOURNAL OF MEDICINE, vol. 348, no. 20, 10 April 2003 (2003-04-10), pages 1953-1966, XP002310169 ISSN: 0028-4793 published online on 10.4.2003 (www.nejm.org) page 1956, left-hand column, paragraph 2 - page 1960, left-hand column, paragraph 2</p>	1-31
Y	<p>WO 02/097114 A (MCSWIGGEN JAMES ; RIBOZYME PHARMACEUTICALS INCOP (US)) 5 December 2002 (2002-12-05) page 4, line 23 - page 5, line 9 page 9, lines 5-15 page 17, lines 14-19 page 35, line 19 - page 36, line 3</p>	1-31
Y	<p>ELBASHIR S M ET AL: "Functional anatomy of siRNAs for mediating efficient RNAi in Drosophila melanogaster embryo lysate" EMBO JOURNAL, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 20, no. 23, 3 December 2001 (2001-12-03), pages 6877-6888, XP002225998 ISSN: 0261-4189 cited in the application page 6881, right-hand column, paragraph 2 - page 6882, left-hand column, paragraph 1 page 6884, left-hand column, paragraphs 3,4 page 6885, left-hand column, paragraph 4 - right-hand column, paragraph 1</p>	1-31
Y	<p>PARRISH S ET AL: "Functional anatomy of a dsRNA trigger: Differential requirement for the two trigger strands in RNA interference" MOLECULAR CELL, CELL PRESS, CAMBRIDGE, MA, US, vol. 6, no. 5, November 2000 (2000-11), pages 1077-1087, XP002226298 ISSN: 1097-2765 cited in the application figures 5,6</p>	1-31
Y	<p>WO 00/44895 A (KREUTZER ROLAND ; LIMMER STEPHAN (DE)) 3 August 2000 (2000-08-03) page 6, line 30 - page 7, line 7 page 18, lines 13-29 claims 27,28,64,65,100,101</p>	1-31
	-/--	

# INTERNATIONAL SEARCH REPORT

Int'l Application No  
PCT/US2004/011320

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 2004/011647 A (CHIRON CORP ; HAN JANG (US); SEO MI YOUNG (US); HOUGHTON MICHAEL (US)) 5 February 2004 (2004-02-05) page 8, paragraph 3 figures 3,4	1-31
P,X	----- DATABASE WPI Section Ch, Week 200424 Derwent Publications Ltd., London, GB; Class B04, AN 2004-248791 XP002310172 & CN 1 465 584 A (UNIV BEIJING JIAOTONG) 7 January 2004 (2004-01-07) abstract	1-31
P,X	----- DATABASE WPI Section Ch, Week 200416 Derwent Publications Ltd., London, GB; Class B04, AN 2004-157625 XP002310173 & CN 1 458 281 A (HUANQIU ZHONGJIA BIOLOGICAL SCI & TECHNO) 26 November 2003 (2003-11-26) abstract	1-31
P,X	----- ZHANG RENLI ET AL: "Inhibiting severe acute respiratory syndrome-associated coronavirus by small interfering RNA." CHINESE MEDICAL JOURNAL (ENGLISH EDITION), vol. 116, no. 8, August 2003 (2003-08), pages 1262-1264, XP002310170 ISSN: 0366-6999 page 1263, right-hand column, paragraph 4 - page 1264, left-hand column, paragraph 1	1-31
P,X	----- HE MING-LIANG ET AL: "Inhibition of SARS-associated coronavirus infection and replication by RNA interference." JAMA : THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. 26 NOV 2003, vol. 290, no. 20, 26 November 2003 (2003-11-26), pages 2665-2666, XP009041436 ISSN: 1538-3598 page 2665, left-hand column, paragraph 2 - page 2666, left-hand column, paragraph 5 -----	1-31

# INTERNATIONAL SEARCH REPORT

...formation on patent family members

Int. Patent Application No  
PCT/US2004/011320

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 02097114	A	05-12-2002	EP 1390472 A2	25-02-2004
			WO 02097114 A2	05-12-2002
			WO 03070193 A2	28-08-2003
			US 2003124513 A1	03-07-2003
			US 2003175950 A1	18-09-2003
			US 2004006035 A1	08-01-2004
			WO 03070912 A2	28-08-2003
			US 2003105051 A1	05-06-2003
			US 2003170891 A1	11-09-2003
			US 2003153521 A1	14-08-2003
WO 0044895	A	03-08-2000	DE 19956568 A1	17-08-2000
			AT 222953 T	15-09-2002
			AU 3271300 A	18-08-2000
			CA 2359180 A1	03-08-2000
			WO 0044895 A1	03-08-2000
			DE 10080167 D2	28-02-2002
			DE 50000414 D1	02-10-2002
			EP 1144623 A1	17-10-2001
			EP 1214945 A2	19-06-2002
			ES 2182791 T3	16-03-2003
			JP 2003502012 T	21-01-2003
			US 2004072779 A1	15-04-2004
			US 2004053875 A1	18-03-2004
			US 2004102408 A1	27-05-2004
			ZA 200105909 A	24-07-2002
WO 2004011647	A	05-02-2004	WO 2004011647 A1	05-02-2004
CN 1465584	A	07-01-2004	NONE	
CN 1458281	A	26-11-2003	NONE	